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SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

EXAMINER	
WILDER, CYNTHIA B	

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1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,797	ZEHENTNER-WILKINSON ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-26* is/are pending in the application.

4a) Of the above claim(s) *17-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/3/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's preliminary amendment filed on 9/22/2005 is acknowledged. Claims 1-4 have been canceled. Claims 5-26 have been added and are pending in the instant invention.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 5-16, drawn to a method for detecting the presence of lung cancer cells, classified in class 435, subclass 91.2.

II. Claims 17-24, drawn to a composition and kit comprising oligonucleotides, classified in class 536, subclass 23.1, 24.33 and 24.32.

III Claims 25-26, drawn to a composition and kit comprising polypeptides and antibodies, classified in class 530, subclass 350.

The inventions are distinct, each from the other because of the following reasons: Inventions II and I are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case, the product comprising oligonucleotides (probes and primers) can be used in a materially different process besides in the method for detecting the presence of lung cancer cells. The oligonucleotides can alternatively be used in methods of nucleic acid sequencing or in methods of nucleic acid cloning or in PCR based mutagenesis assay or in aptamer or

antisense studies. A search burden exists if the different inventions are searched together because the searches of the different inventions are not coextensive. Specifically a search of the product of group II comprises an extensive search in patent and non-patent literatures that may or may not have knowledge of the product's use in a method for detecting the presence of lung cancer cells in a biological sample. Moreover, even if the oligonucleotide products were known, the method of detection using the product may be novel and unobvious in view of the preamble or active steps. Accordingly, the different invention requires different fields of search.

Inventions III and I are directed to an unrelated product and process. Product and process inventions are unrelated if it can be shown that the product cannot be used in, or made by, the process. See MPEP § 802.01 and § 806.06. In the instant case, the product comprising polypeptides and antibodies can be used in protein binding assays such as e.g., in Western Blotting assays or in immunoprecitation assays or immunoasays, rather than a PCR amplification reaction to determine mRNA expression. A search burden exists because the different invention comprises non-overlapping subject matter that requires different fields of search.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the polypeptides, which are composed of amino acids, and polynucleotides, which are composed of purine and pyrimidine units, are structurally distinct molecules; any relationship between a polynucleotide and polypeptide is dependent upon the

information provided by the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Furthermore, the information provided by the polynucleotide of group II can be used to make a materially different polypeptide than that of group III. For example, a nucleic acid which hybridizes to SEQ ID NO: 5, even under stringent conditions, encompasses molecules which contain point mutations, splice sites, frameshift mutations or stop codons which would result in use of a different open reading frame, and thus encode a protein that lacks any significant structure in common with SEQ ID NO. 6. In addition, while a polypeptide of group III can made using the polynucleotides that fall within the scope of group II, it can also be recovered from a natural source using by biochemical means. For instance, the polypeptide can be isolated using affinity chromatography. For these reasons, the inventions of groups II and III are patentably distinct.

Furthermore, searching the inventions of groups II and III would impose a serious search burden. In the instant case, the search of the oligonucleotides and the polynucleotides/antibodies are not coextensive. The inventions of Groups II and III have a separate status in the art as shown by their different classifications. In cases such as this one where descriptive sequence information is provided, the sequences are searched in appropriate databases. There is search burden also in the non-patent literature. Prior to the concomitant isolation and expression of the sequence of interest there may be journal articles devoted solely to polypeptides, which would not have described the oligonucleotide. Similarly, there may have been "classical" genetics papers which had no knowledge of the polypeptide but spoke to the gene. Searching,

therefore is not coextensive. As such, it would be burdensome to search the inventions of groups II and III together.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

3. Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the

rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

4. During a telephone conversation with Julie Urvater on May 7, 2007 a provisional election was made with traverse to prosecute the invention of Group I, claims 5-16. Affirmation of this election must be made by applicant in replying to this Office action. Claims 17-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Double Patenting

6. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7. Claims 5-16 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-9, 17-18, 20, 21 and 22 of copending Application No. 11/392479. The claims of the instant invention and copending application 11/392479 are drawn to a method for detecting the presence of lung cancer cells in a biological sample comprising the steps of detecting the level of mRNA in the biological sample of two or more cancer associated markers selected from the group consisting of L762P or L550S or L587S or L984P or L552S OR L763P; and comparing the level of expression detected in the biological sample for each marker to a predetermined cut-off value for each marker; wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the

biological sample. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 5-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson et al *(20020172952, Filing date July 2001)* in view Wang et al {Wang et al ('329), herein} *(20020052329, filing date December 2000)* and Wang et al {Wang et al ('012), herein} *(20020099012, filing date June 2001)* and further in view of Edwards and Gibbs *(PCR Methods and Applications, vol. 3, pages S65-S75, 1994)*.

Regarding claims 5 and 6, Henderson et al teach a method for detecting the presence of lung cancer cells in a biological sample comprising the steps of (a)

detecting the level of mRNA expression in biological samples of one or more cancer associated markers; and (b) comparing the level of mRNA expression detected in the biological samples for each of the markers to a predetermined cut-off value for each marker; wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the biological sample (see 0034-0035, 1284-1287, 1295, 1302, 1307, 1321, 1345 and 1349). Henderson further teaches wherein the cancer-associated markers comprise L984P (paragraph 1376, 1382-1390) and L552P (see paragraphs 1493-1495). Henderson also discloses the cDNA sequence for L550S (see 0116), L552 (see 0845) and L984P (see 0930).

Wang et al ('329) teach a method similar to that of Henderson et al for detecting the presence of lung cancer cells in a biological sample comprising the steps of (a) detecting the level of mRNA expression in biological samples of one or more cancer associated markers; and (b) comparing the level of mRNA expression detected in the biological samples for each of the markers to a predetermined cut-off value for each marker; wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the biological sample (see 0026-0027; 0504, 0514, 0603, 0616, 0618-0619, 0642, 0644, 0650-0656). Wang et al further teach wherein the cancer-associated markers comprise L762P and L763P (paragraphs 0661 and 0662). Wang et al also teach the cDNA sequence for L762P and L763P (see 0187 and 0189).

Wang et al ('012) teach a method similar to that of Henderson et al and Wang et al ('329) for detecting the presence of lung cancer cells in a biological sample comprising the steps of (a) detecting the level of mRNA expression in biological samples of one or more cancer associated markers; and (b) comparing the level of mRNA expression detected in the biological samples for each of the markers to a predetermined cut-off value for each marker; wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the biological sample (see 0026-0027, 0511, 0532-0533, 0763, 0776-0778). Wang et al further teach wherein the cancer-associated markers comprise L587S (paragraph 0805).

The references do not expressly teach wherein two or more cancer-associated markers are detected in the same biological sample. However, methods of detecting multiple targets in a biological sample are well known in the prior art. For example, Edwards and Gibbs teach a method for simultaneously detecting multiple targets using multiplex PCR techniques. Edwards and Gibbs teach that multiplex PCR is a useful tool because it includes internal controls, allows the indication of template quantity and quality, is less expensive in terms of time and reagents, and exhibit great flexibility in experimental design and in overcoming limiting primer kinetics and fragment competition. Therefore, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modify the detection method of Henderson et al and Wang et al ('329) and Wang et al ('012) to encompass steps of multiplex PCR as taught by Edwards and Gibbs for the obvious benefit of

simultaneously detecting multiple targets from a single biological sample in a single assay and for the additional advantages taught by Edwards and Gibbs, such as flexibility of experimental design and increase reduction in expense and time that is associated with multiplex PCR.

Regarding claim 7, Henderson et al teach wherein the step (a) comprises detecting the level of mRNA expression using a nucleic acid hybridization technique (see 0034, 1107, 1115 and 1321).

Regarding claims 8 and 9, Henderson et al teach wherein the step (a) comprises detecting the level of mRNA expression using a nucleic acid amplification method selected from the group consisting of PCR, LCR, SDA and NASBA (paragraph 1153).

Regarding claim 10, Wang et al ('329) teach a sequence that is 100% identical to the sequence of SEQ ID NO: 2 (see SEQ ID NO: 161).

Regarding claim 11, Henderson et al teach a sequence that is 100% identical to the sequence of SEQ ID NO: 6 (see SEQ ID NO: 789 and Example 1).

Regarding claim 12, Wang et al teach a sequence that is 100% identical to the sequence of SEQ ID NO: 26 (see SEQ ID NO: 473).

Regarding claim 13, Henderson et al teach a sequence that is 100% identical to the sequence of SEQ ID NO: 4 (see SEQ ID NO: 1871 and Example 9).

Regarding claim 14, Henderson et al teach wherein the cancer is a small cell lung cancer or a non-small cell lung cancer (paragraph 1346).

Regarding claim 15 and 16, Henderson et al teach wherein the biological sample is selected from the group consisting of blood sera, sputum, urine and/or tumor biopsies (1284).

Conclusion

11. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637

7/22/2007